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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,414	01/30/2002	Hironobu Murase	4296-146 US	2128

7590 12/03/2003

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EXAMINER	
MCINTOSH III, TRAVISS C	
ART UNIT	**PAPER NUMBER**
1623	12

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/937,414	MURASE ET AL.	
	Examiner	Art Unit	
	Traviss C McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-21* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Amendment filed September 11, 2003 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claims 10-21 have been amended.

Claims 1-9 have been canceled.

Remarks drawn to rejections of Office Action mailed March 11, 2003 include:

Claim objections: which have been overcome by applicant's amendments and have been withdrawn.

Obvious Double Patenting rejection: which has been overcome by applicant's amendments and has been withdrawn.

112 1st paragraph rejections: which have been maintained for reasons of record.

112 2nd paragraph rejections: which have been overcome by applicant's amendments and have been withdrawn.

102(b) rejection: which has been overcome by applicant's amendments and has been withdrawn.

103(a) rejection: which has been overcome by applicant's amendments and has been withdrawn.

An action on the merits of claims 10-21 is contained herein below.

The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Specification

The disclosure is objected to because of the following informalities: the specification contains errors in the examples and refers the reader to the wrong tables. For example: page 27, line 18 states that "it is clearly noted from table 4 that the pigment sedimented by the UV light was lightened", but table 4 contains information about cell growth, not color or pigmentation change. Table 3 contains this information. Likewise, page 28, line 24 states that the results showing the breeding ratios of the cells are show in table 3, however, table 3 is drawn to pigmentation variances, and table 4 contains breeding rations. It is noted that these two examples are not inclusive of the complete list of inaccuracies, just examples of certain inaccuracies noticed.

Appropriate correction of all inaccuracies is required.

Claim Objections

Claim 18 is objected to because of the following informalities: the claim repeats "the" two times in a row in the first line. (i.e., "a method for preventing the the formation...") Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 10-15 and 18-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant disclosure is not seen to be sufficient to enable the use of the chromanol glycoside of formula 1 to **prevent and cure** the conditions as claimed, such as: **cutaneous inflammation, inflammation caused by ultraviolet light, the deposition of pigment in the skin, and the formation of wrinkles and sags caused by ultraviolet light,** without undue experimentation

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in ***In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)***. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims – The nature of the invention

Claim 10 of the instant application is drawn to a method of preventing and curing cutaneous inflammation. Claim 12 is drawn to a method of preventing and curing inflammation caused by ultraviolet light. Claim 14 is drawn to preventing and allaying the deposition of pigment in the skin. Claim 18 is drawn to a method of preventing the formation of wrinkles and sags caused by ultraviolet light.

The state of the prior art

Chromanol glycosides are known in the art to be useful as hypoglycemic agents in treating diabetes and diabetic complications as seen in JP-01-305,097, and also to be useful as pH stabilizers, antioxidants, radiation protecting agents, and for treating inflammatory intestinal diseases as seen in JP-11-279,192 and US Patent 5,478,812. At present, there are no known agents capable of preventing and curing cutaneous inflammation, inflammation caused by ultraviolet light, the deposition of pigment in the skin, and the formation of wrinkles and sags caused by ultraviolet light.

The level of predictability in the art

The examiner acknowledges the probability and predictability that the active agent, which is a chromanol glycoside, has efficacy in *treating* certain conditions associated with various skin conditions due to it's art recognized antioxidant properties, however the art is silent with regard to the predictability of effectively *preventing and curing* cutaneous inflammation, inflammation caused by ultraviolet light, the deposition of pigment in the skin, and the formation of wrinkles and sags caused by ultraviolet light, by administering the chromanol glycoside as the active agent.

The amount of direction provided by the inventor

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to use the claimed method commensurate in the scope with the instant claims. There is a lack of data and examples which adequately represent the scope of claims as written. The examiner notes, there has not been provided sufficient instruction or sufficient methodological procedures to support the alleged efficacies instantly asserted.

The existence of working examples

The working examples set forth in the instant specification are directed to various tests involving ultraviolet light (UVB) on fibroblasts to determine survival ratios, cornified cells to determine the repression of IL-1α production, on the backs of shaved guinea pigs to determine pigment sedimentation, and on fibroblasts for determining cell growth/replication. The results show that the survival/prevention/curing percentage was not 100% in any instance (see tables). Specifically, Table 1 shows that the survival ration of the cells was higher with the claimed compounds than with the control, but none of the compounds produced 100% survival ratio, thus the cells were not prevented from dying. Table 2 shows that IL-1 levels produced were repressed compared to the control group, but none of the test compounds were able to limit the production to 0%, thus the cells were not prevented from producing IL-1. There is no evidence of preventing or curing anything.

There has not been provided sufficient evidence which would warrant the skilled artisan to accept the data and information provided in the working examples as correlative proof that a healthy individual would never become afflicted with or be effectively cured from any cutaneous

inflammation, inflammation caused by ultraviolet light, deposition of pigment in the skin, and formation of wrinkles and sags caused by ultraviolet light, if subjected to the instantly claimed therapy.

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable the use of the chromanol glycoside claimed to prevent and cure the claimed conditions without undue experimentation. One skilled in the art could not use the entire scope of the claimed invention without undue experimentation.

Reasonable guidance with respect to prevention and curing of anything relies on quantitative analysis from defined populations which have been successfully pre-screened and are predisposed to particular types of the conditions. This type of data might be derived from widespread genetic analysis, cancer clusters, or family histories. The essential element towards the validation of a preventive therapy or cure relies on the ability to test the drug on subjects monitored in advance of clinical conditions and *link* those results with subsequent histological confirmation of the presence or absence of disease. This irrefutable link between antecedent drug treatment and subsequent knowledge of the prevention of the disease is the essence of verification of a valid preventive agent.

It is noted that applicants argue that undue experimentation is not required to administer an effective amount of a chromanol glycoside to ameliorate cutaneous inflammation and the formation of wrinkles and sags caused by ultraviolet light. The examiner agrees with this

statement, however, applicants are not claiming methods of *ameliorating* conditions, but rather methods of *preventing and curing* conditions, and as set forth supra, applicants are not enabled for the prevention or curing of any conditions.

Claims 11, 13, 15, 17-19, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claims 11, 13, 15, 17, 19, and 21 all further limit the methods from which they depend by providing that "said chromanol glycoside is A, B, C, and D" wherein A, B, C, and D are the specific compounds as listed in the claims. However, it is unclear how the chromanol glycoside can be all of the compounds listed, that is how can the chromanol glycoside be A, B, C, and D? The claim should be drafted to provide that the chromanol glycoside can alternatively by different members of the group using language such as "selected from the group consisting of A, B, C, and D" or "selected from A, B, C, or D", not, "wherein the glycoside is A, B, C, and D". Correction is required.

Claim 18 is indefinite wherein the claim is drawn to a "method for preventing the the formation of wrinkles and sags caused by ultraviolet light in a mammal...", but the claim does not set forth in what the wrinkles and sags are in, the skin, the wrinkles of the brain, sags in the liver? Clarity is respectfully requested. The examiner has interpreted the claim as wrinkles and sags in the skin.

Claim Rejections - 35 USC § 103

Claims 10-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murase et al. (US Patent 5,478,812) in view of Kennedy et al. (US Patent 6,165,445).

Claims 10-21 are drawn to methods of treating various conditions by administering the art known chromanol glycoside of formula 1 to a mammal. The conditions treated, such as cutaneous inflammation, inflammation caused by ultraviolet light, the deposition of pigment in the skin, whitening the skin, the formation of wrinkles and sags caused by ultraviolet light, and promoting the growth of cells, are seen to share the common requirement of having an antioxidant as the active agent.

Murase et al. teach of chromanol glycosides which are coextensive in scope with the compound of formula 1 of the instant application. Murase et al. teach that their chromanol glycosides are water-soluble antioxidants having excellent stability and usable as a solution making use of the chroman ring of outstanding antioxidant activity (column 1, lines 61-67). What is not taught is to treat the specific conditions as claimed in the instant application.

Kennedy et al. teach that inflammation is mediated by the activation of the transcription factor NF-κB, which in turn causes an increase in cellular production of pro-inflammatory cytokines, such as IL-1, and recently, antioxidants have been found to inhibit NF-κB and thus the subsequent cytokine secretion (column 6, lines 49-58), thus administering antioxidants, are effective in treating inflammatory diseases.

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer the chromanol glycoside of Murase et al. to a patient to treat inflammation (and other antioxidant mediated disorders) because Murase et al. teach that their compound has

antioxidant properties, and inflammation is taught by Kennedy et al. to be treated by antioxidants. One would have been motivated to use the chromanol glycoside of Murase et al. because Murase et al. teach that their glycosidated substances have various advantages, such as solubility in water, enhanced chemical stability, and increased biological activity as compared to non-glycosidated substances (column 3, lines 6-10). The conditions which are claimed to be treated are known in the art to be effectively treated by administering antioxidants, and the chromanol glycoside is taught to have antioxidant activity, thus it would have been obvious to one of ordinary skill in the art to administer the chromanol glycoside to the antioxidant mediated conditions.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 703-308-9479. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

James O. Wilson
Supervisory Patent Examiner
Art Unit 1623

Traviss C. McIntosh III
November 19, 2003